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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/721,839
Filing Date: November 25, 2003
Appellant(s): MAURY ET AL.

Steven L. Highlander
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed October 10, 2006 appealing from the Office action mailed April 18, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

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(8) Evidence Relied Upon

WO 02/085401 A1 (Lehrer et al.) October 31, 2002.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 9, 18-24, 27, 28, 34-38, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Lehrer. These claims are directed to methods of reducing the infectivity of a virus, particularly HIV, through administration of the peptides of SEQ ID NO: 31 or 32. These peptides are examples of a group of antimicrobial peptides known as retrocyclin, or theta, defensins. The linear sequences of these peptides have been disclosed as follows:

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
SEQ ID NO: 31	G	I	C	R	C	L	C	R	R	G	V	C	R	C	I	C	G	R

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
SEQ ID NO: 32	G	I	C	R	C	I	C	T	R	G	F	C	R	C	I	C	G	R

The number above the letter representing each amino acid residue corresponds to the residue's position in the sequence. Because the peptides are circular in nature, they can also be represented as follows:

	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	1	2	3
SEQ ID NO: 31	R	C	L	C	R	R	G	V	C	R	C	I	C	G	R	G	I	C

	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	1	2	3
SEQ ID NO: 32	R	C	I	C	T	R	G	F	C	R	C	I	C	G	R	G	I	C

As the two peptides are circular in nature, this linear expression of the sequence is equally valid.

Lehrer teaches the making and use of theta defensins comprising an amino acid sequence formed from any combination of two nonapeptides selected from those disclosed as SEQ ID NOs: 19-64 in the reference. See e.g., claim 6. The reference additionally teaches that these defensins may be administered to a subject with a viral infection, facing exposure to viral infection, including infection by HIV. Pages 13-14. The reference teaches that the defensins may be applied topically (page 13, lines 31-32), and may be applied in combination with other antiviral agents (pages 17-18). While the reference does not teach the specific dosages for the defensins, the reference indicates that such dosages would vary based on several factors (page 16, lines 24-30), and thereby indicating that the claimed dosages would be obvious based on routine optimization of the disclosed compositions.

It is noted that the reference does not verbatim teach the use of the peptides of SEQ ID NOs: 31 and 32 of the present application. However, as indicated above, the reference teaches the combination of any of the specifically disclosed nonapeptides for the formation of a theta defensins for use in the indicated methods. Thus, while the reference does not lay out each of the indicated defensin peptides individually, by setting forth the nonapeptides from which they are made, the reference nonetheless sets forth a specific set of defensin peptides that may be immediately envisaged by those of ordinary skill in the art. This group of disclosed peptides includes each of the peptides formed by each combination of two of the nonapeptides disclosed on pages 7-8 of the reference.

Among the nonapeptides disclosed by the reference are those of SEQ ID NOs: 18, 27, and 34. The sequences of these nonapeptides are represented as follows:

18 = R - C - I - C - T - R - G - F - C,

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27 = R - C - L - C - R - R - G - V - C, and

34 = R - C - I - C - G - R - G - I - C.

Placing nonapeptide 27 first (as there is no correct beginning for a cyclic peptide), the following represents an alignment of the defensin comprising peptides 27 and 34 of Lehrer with SEQ ID

NO: 31 of the present application:

Lehrer 27 and 34	R - C - L - C - R - R - G - V - C	R - C - I - C - G - R - G - I - C													
	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	1 2 3													
SEQ ID NO: 31	R - C - L - C - R - R - G - V - C - R - C - I - C - G - R - G - I - C.														

As can be seen, the defensin represented by this peptide is identical to SEQ ID NO: 31.

Similarly, an alignment of the defensin of Lehrer peptides 18 and 34 (respectively) with that of SEQ ID NO: 32, shows that SEQ ID NO: 32 is also among the defensins contemplated by the

Lehrer reference:

Lehrer 18 and 34	R - C - L - C - T - R - G - F - C	R - C - I - C - G - R - G - I - C													
	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	1 2 3													
SEQ ID NO: 32	R - C - I - C - T - R - G - F - C - R - C - I - C - G - R - G - I - C.														

Thus, the reference renders obvious the peptides of SEQ ID NO: 31 and 32. Moreover, because the reference teaches the use of such peptides in methods according to the present claims, the reference also renders the claimed methods of using these peptides obvious.

Those of ordinary skill in the art would have had a reasonable expectation of success in the disclosed use of such peptides based on the suggestion in the reference that each of the defensin peptides derived from the disclosed nonapeptides would be useful in the claimed methods. See e.g., pages 7 and 13-14. Moreover, while the reference indicates that certain derivatives of defensins (those comprising tyrosine) were marginally or ineffective against some viruses tested (page 23, lines 25-29), none of such peptides are included in the sequences

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disclosed on pages 7-8. Thus, those of ordinary skill in the art would have had a reasonable expectation of success in the use of each of the defensins contemplated by the disclosures on pages 7-8, including the present defensins of SEQ ID NOs: 31 and 32, as antiviral agents.

The rejection of the claims based on the teachings of Lehrer should therefore be maintained.

(10) Response to Argument

The Appellant provides two arguments in traversal of the rejection. In essence, the first of these arguments is that the Lehrer reference fails to provide motivation for the selection of the defensin peptides of SEQ ID NO: 31 and 32 from the genus of peptides disclosed therein. The second argument is an assertion that the Examiner has not considered other variable relevant to the consideration of the differences between the prior art and the claimed invention. These arguments should not be found persuasive for the reasons below.

1) There are adequate teachings to render the claimed methods obvious.

The Appellants first argument that the rejection should not be maintained is that the Lehrer reference teaches a genus of peptides, and provides no specific motivation for the selection of the defensins of SEQ ID NO: 31 and 32 specifically. The Appellant relies on decisions such as *In re Deuel*, 34 U.S.P.Q. 2d 1210; *In re Ruschig*, 145 U.S.P.Q. 274; and *In re Bell*, 26 U.S.P.Q. 2d 1529 in support of their argument that the disclosure of the genus in Lehrer does not render obvious these specific peptides.

It is noted that each of the *Deuel* and *Ruschig* cases deals with situations where there has been no specific guidance towards the claimed species in the prior art references. In both cases,

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the prior art references relied upon disclosed only a generic group of compounds. See e.g., *In re Deuel*, 34 U.S.P.Q.2d at 1214-15; and *In re Ruschig*, 145 U.S.P.Q. at 283-84. In the *Ruschig* case, the prior art did not even disclose the uses of the indicated compounds. Such is not the present case. As was described above, the teachings of Lehrer specifically set forth the sequences to be combined to form the desired defensin peptides, including the sequences that form the peptides of interest in the present case. Because Lehrer provides these sequences, the reference clearly contemplates a genus of peptides identified by their sequences, any one of which would have been immediately envisaged by those of ordinary skill in the art upon the reading of the reference. Thus, unlike the situation in either *Deuel* or *Ruschig*, there are specific teachings rendering SEQ ID NO: 31 and 32, in addition to other defensin peptides, obvious. While the reference discloses a genus of peptides, it does so through providing the specific sequences used to make the individual species it contains.

With respect to the *Bell* decision, it is noted that the claims in that decision required an additional limitation over what was disclosed in the prior art. Specifically, the claims at issue in that case read only on human DNA, whereas the prior disclosed DNA sequences encoding the protein of interest generally, but provided no guidance as to the human DNA sequences. In the present case, the claims require only that the peptides have anti-viral activity. The Lehrer reference indicates that each of the specifically contemplated peptides would have the desired function. In the present case, unlike in *Bell*, there is nothing to distinguish the claimed species from those contemplated in the prior art reference. Thus, those of ordinary skill in the art would have had motivation and a reasonable expectation of success in the use of each of these contemplated peptides, including those of SEQ ID NOs: 31 and 32.

The Appellants reliance on these cases to show that the present peptides are not an obvious species of the genus disclosed by the prior art is therefore misplaced. These cases indicate that the claimed species may not be obvious in situations wherein there has either been no identification or contemplation of the specific species at issue, or where the species at issue have characteristic distinguishing them from a previously known genus. As indicated above, neither situation applies in the present case.

The Appellant also asserts that the size of a genus that is disclosed by a reference is a factor to be considered. The Appellant asserts that there is no motivation to arrive at either SEQ ID NO: 31 or 32 from the 2116 peptides disclosed by Lehrer. However, the Federal Circuit Court of Appeals has also stated that "it is not the mere number of compounds in this limited class which is significant here but, rather, the total circumstances involved." See, *In re Baird*, 29 USPQ2d 1550, at 1552 (1994). In the present case, the reference teaches a number of specific nonapeptides that may be combined, and indicates that any two of these peptides may be combined to result in an operable retrocyclin defensin. From these teachings, those of ordinary skill in the art would have been able to immediately envisage each of the various resulting retrocyclin defensins. Thus, while the reference provides teachings rendering obvious a genus of 2116 peptides (representing a combination of any two of the peptides listed on page 7-8 of the reference), because the reference provides the sequences, each of these peptides is individually obvious. Further, the reference indicates that each of these peptides would be operable, thus providing both motivation and a reasonable expectation of success. Thus, while the size of the genus may be a factor, in the present case the totality of the circumstances indicates that the present claims drawn to SEQ ID NOs: 31 and 32 are nonetheless obvious embodiments of the

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genus disclosed by Lehrer. This is due to the teachings of that reference permitting those of ordinary skill in the art to immediately envisage each of the members of that genus including the peptides of interest.

In view of the above, the Appellant's arguments that there is inadequate motivation to select SEQ ID NO: 31 and 32 from the genus disclosed by Lehrer should not be found persuasive, and the rejection affirmed.

2) The other relevant factors support a finding of obviousness.

The Appellant next asserts that the Examiner overlooked other variables and factors in the consideration of the teachings of the prior art. In particular, the Appellant indicates that there is unpredictability the relevant technology (i.e. the modification of proteins). This argument should not be found persuasive because, while it is accepted that there is unpredictability in the art of protein modification in general, there is nothing in the art or the record to show that these considerations apply in the present situation. In particular, as was noted above, the teachings of Lehrer indicate that there are particular subsets of defensin derivatives with variable operability (those comprising tyrosine substitutions). However, the peptides listed on pages 7-8 are drawn specifically from substitutions found in nature (and therefore presumably operative). Moreover, as was noted above, none of the sequences disclosed on these pages include those with the inoperative tyrosine substitutions referred to on page 23 of the reference. Thus, those of ordinary skill in the art would have had a reasonable expectation of success with respect to the use of defensins having the sequences provided on pages 7-8, and would not have considered the

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general unpredictability of the art of protein modification to be a factor with respect to the use of these envisaged peptides.

Moreover, it is noted that the Appellant has provided no evidence in support of their assertion that such factors would have colored the expectations of those of ordinary skill in the art with respect to these peptides. Appellant has provided no showing that any of the peptides suggested by the reference fail to have the desired functionality. Thus, in view of the discussion above, and the lack of any evidence in support of the Appellants arguments as they are drawn to the specific peptides of relevance, these arguments should not be found persuasive, and the rejection should be affirmed.

With respect to the unpredictability of the uses of the peptides against HIV, Appellants arguments should not be found persuasive. While there is unpredictability in the art of treating and preventing HIV, the present claims require only a reduction of the infectivity of (a) enveloped viruses in general, and (b) of HIV in particular. The teachings of Lehrer demonstrate that several defensins derived from the sequences of pages 7-8 are generally effective in the inhibition of HIV infectivity. See e.g., page 23 and Figure 9. Such teachings would also have provided those of ordinary skill in the art with a reasonable expectation of success for the use of the other peptides comprising the disclosed sequences. Moreover, because the claims do not require actual pharmaceutical effect, and as many compounds that are eventually found not to be suitable pharmaceuticals nonetheless provide in vitro reduction of HIV infectivity, the Appellants assertion that unpredictability in the art of treating HIV undercuts the obviousness of the claimed peptides should not be found persuasive. This is even more true in the present case as the Appellant has not demonstrated that the peptides of SEQ ID NO: 31 or 32 are more

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effective than the other peptides envisaged by Lehrer, or even capable of pharmaceutical effect in vivo.

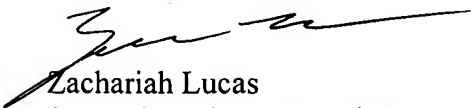
For each of these reasons, Appellant's arguments should not be found persuasive, and the rejection should be affirmed.

(11) Related Proceeding(s) Appendix


No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

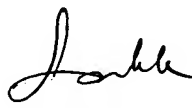
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